

Morphea presenting as widespread oedema

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Acute localized scleroderma (morphea) can present as severe generalized oedema with rapid weight gain and oliguria. The putative mechanism is increased capillary permeability.

CASE HISTORY

A woman of 67 was referred to the renal service for investigation of severe and increasing peripheral oedema which had not responded to treatment with diuretics. Her weight had risen by 12 kg in a few weeks. On close questioning she indicated that the skin of her swollen legs had become abnormal in texture, 'hard', and she had also noticed hardening of the skin of the forearms and lower abdomen. 7 years previously seronegative rheumatoid arthritis had been diagnosed, mainly affecting her hands; this had responded to weekly methotrexate, which she was still taking.

There was sacral and pretibial oedema, with abdominal swelling; the lungs were normal and jugular venous pressure was not raised. She had striking dermatographia, acrosclerosis and hardening of the skin of both legs. Dipstick testing of urine revealed neither proteinuria nor haematuria. On admission, plasma sodium was 138 mmol/L, potassium 3.9 mmol/L, albumin 28 g/L, urea 4.7 mmol/L and creatinine 76 µmol/L. C-reactive protein was 70 mg/L. Haemoglobin was 11.9 g/L with normal white cell count and differential; platelet count was $454 \times 10^9/L$. Results of the following were all normal: plasma glucose, calcium, phosphate, bilirubin, alanine aminotransferase, alkaline phosphatase, immunoglobulins and protein electrophoresis, and complement C3 and C4; clotting tests; thyroid function tests; bone marrow biopsy; and abdominal CT scan (apart from generalized oedema). An echocardiogram showed normal left ventricular function but there was some dilatation of the right ventricle with moderate tricuspid regurgitation. Initial urine volume was only

500 mL/day, though creatinine clearance was normal. Albuminuria remained undetectable, but she had tubular proteinuria; 24-hour urinary sodium excretion was very low (12 mmol/24 h) and remained so for several weeks; urine osmolality was 982 mosm/kg, with plasma osmolality 294 mosm/kg. Colloid oncotic pressure was slightly reduced at 19 mmHg (normal range 20–23). After admission she gained a further 20 kg (about 1 kg/day), despite fluid restriction. Further investigations showed serum aldosterone normal, renin about twice the upper limit of normal, rheumatoid factor negative, antinuclear antibody (ANA) weakly positive at 1:20, anti Ro, La, Sm, RNP, Jo-1 and SCL070 all negative. Urinary cortisol was normal.

A diagnosis of morphea was suggested and was confirmed by skin biopsies. She was treated first with methylprednisolone, then with oral steroids and a trial of penicillamine. The skin disorder stabilized and the oedema subsided over a few months. Renal function, which did not change during the hospital admission, remained stable during 2 years of follow up with plasma creatinine around 90 µmol/L and an isotopic glomerular filtration rate of 60 mL/min/m². She has required treatment for hypertension, currently well controlled on two drugs. Her albumin and haemoglobin are now normal. There has been no recurrence of the peripheral oedema.

COMMENT

This patient seems to have had a widespread increase in capillary permeability in association with her acute morphea, triggering avid renal sodium retention. The case is unusual in that the patient was not particularly unwell (in contrast to patients with 'capillary leak syndrome', who are usually very sick and hypotensive, even shocked¹), and the onset of the syndrome was gradual. The oedema was caused by increased dermal capillary permeability, which led to a barely evident reduction in circulating volume. The renal response was to conserve salt and water, explaining the persistently low urinary volumes and low urinary sodium. The high plasma renin levels also reflect volume depletion.

Morphea can be localized or, as in this case, widespread. It is more common in women than men and in most cases is associated with ANA positivity. The condition is distinguished from scleroderma by the absence of Raynaud's phenomenon and systemic disease. Morphea on the background of seronegative rheumatoid arthritis is unusual, and perhaps this case should be viewed as an 'overlap syndrome'. In scleroderma oedema is a recognized complication, and there is evidence of abnormal microvasculature in this condition with broadening and splitting of the basal lamina of capillaries². During the oedematous phase of both morphea and scleroderma, concentrations of certain cytokines are

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high, subsiding as the disease moves to a more chronic phase³. These cytokines are probably the cause of the abnormal capillary permeability and oedema. Tubular proteinuria, which was present in our patient, has been reported in association with high levels of circulating cytokines in other inflammatory diseases⁴. Oedema, either localized or generalized, is commonly seen in the rheumatic diseases and presumably likewise results from a cytokine-induced vascular leak. In dermatomyositis the oedema may be localized around the eyes or may be generalized, with substantial weight gain⁵. In rheumatoid arthritis, localized limb oedema is a well-known phenomenon; it has also been reported in systemic lupus erythematosus⁵ and diffuse systemic sclerosis⁶. In many cases it responds well to treatment with steroids. Widespread systemic vascular leakage is seen in patients treated with interleukin 2, interferon α and immunotoxins, and commonly it is the dose-limiting factor in these treatments⁷. Spontaneous 'systemic capillary leak syndrome' is very rare and tends to be associated with monoclonal gammopathy, which was excluded in our patient; in this syndrome there is episodic severe hypotension and haemoconcentration as well as profound hypoalbuminaemia¹. The primary cause seems to be a circulating toxic factor that increases capillary permeability, perhaps by causing endothelial cell apoptosis⁸.

The treatment of scleroderma is made difficult by the variability of its natural course and uncertainty as to its pathogenesis⁹. Immunosuppressant agents such as methotrexate have been used, with encouraging results in one small trial¹⁰. Because our patient's symptoms developed while she was taking methotrexate, she was treated initially with the antifibrotic agent penicillamine. Spontaneous improvement of scleroderma/morphea is well recognized, so we cannot be sure that the course of her illness was affected by the treatment.

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Incidental splenic artery aneurysm

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Splenic artery aneurysms occur in approximately 1% of the population and are usually incidental findings¹. Rupture carries a substantial mortality².

CASE HISTORY

A woman of 76 with a history of hypertension, pulmonary embolus and rectal adenocarcinoma was found to have a splenic artery aneurysm (SAA) of 3–4 cm on routine surveillance ultrasound scan of the liver. She had never been pregnant. At no point did she have any symptoms or signs of the aneurysm, such as abdominal pain or an abdominal mass. Initial contrast runs of the coeliac axis showed a 4 cm aneurysm at the splenic hilum and also a 1.5 cm aneurysm of the left hepatic artery (Figure 1). The splenic artery aneurysm was not suitable for embolization because its position close to the splenic hilum allowed for little collateral blood supply and post-embolization infarction of the spleen was likely. The hepatic artery aneurysm was successfully embolized with thrombogenic steel coils. The following day, after immunization against *Streptococcus pneumoniae* and *Haemophilus influenzae* type b, she underwent splenectomy and removal of the SAA. Sixteen months postoperatively she was in good health.

COMMENT

The incidence of SAA is quoted as being 0.7% of the population but necropsy studies have given rates as high as 10%². The incidence of SAA in females is four times the

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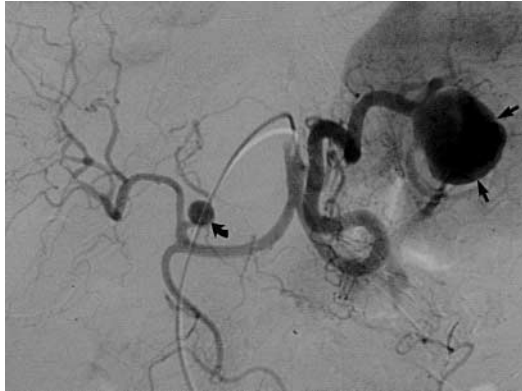


Figure 1 Coeliac angiogram showing large splenic artery aneurysm (straight arrows) and smaller left hepatic artery aneurysm (curved arrow)

rate in males. This difference, thought to be due to the hormonal and haemodynamic changes associated with pregnancy, is not seen with other visceral artery aneurysms³. SAA is the second commonest intra-abdominal aneurysm after aortoiliac aneurysms; usually there are no symptoms and only 27% present with abdominal pain^{2,4}.

Incidental diagnosis of SAA is becoming increasingly frequent with the growing use of angiograms, CT scans and ultrasonograms for investigation of other lesions². The peak age of detection is the sixth decade¹. The cause of these aneurysms is uncertain, but increased blood flow through the splenic artery may be a factor. Portal hypertension with large portasystemic shunts causes a rise in portal blood inflow volume which is thought to increase the aneurysmal propensity of the splenic artery^{1,2,5}. Arteriosclerosis is the commonest pathological finding and is probably a post-aneurysmal phenomenon rather than a primary cause of the aneurysm. Half the ruptures occur in pregnant women and the mortality after rupture is 70–90%⁶.

For patients aged over 60 years with no symptoms and with aneurysms less than 20 mm in diameter, conservative management with CT scans every six to twelve months is advocated⁴. Treatment is indicated for aneurysms that cause symptoms, those more than 30 mm in diameter, and those detected in women who are pregnant or of childbearing age: these are groups with an increased risk of rupture^{2,3}. There is no clear advice on how to manage aneurysms between 20 and 30 mm.

The favoured method of treatment at present is embolization. However, there is little follow-up information for this method and recurrence is a possible long-term hazard³. When embolization is difficult or contraindicated by the proximity of the aneurysm to the spleen (with risk of splenic infarction) the options are open or laparoscopic surgery with ligation of the splenic artery, excision of the aneurysm with reanastomosis of the artery or splenectomy with removal of the aneurysm³.

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Hyponatraemia without hypovolaemia

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Hyponatraemia is commonly attributed to the syndrome of inappropriate antidiuretic hormone secretion (SIADH), but other causes must first be excluded.

CASE HISTORY

A man of 66 attended the emergency department because of confusion, unsteadiness, slurred speech, nausea and symptoms of prostatic obstruction. For the past month he had been troubled by fatigue and myalgia, and for ten days he had been experiencing nausea (treated by his general practitioner with prochlorperazine). Previously he had been well, and prochlorperazine was his only current medication. On examination he was not obviously dehydrated. Blood pressure was 120/80 mm Hg, with no postural drop. There were no focal neurological signs and no physical abnormalities were detected elsewhere, including the prostate. Initial investigation disclosed pronounced hyponatraemia (sodium 110 mmol/L), low serum osmolality (261 mosm/kg) and inappropriately high urine osmolality (462 mosm/kg). Other blood results, including prostate specific antigen,

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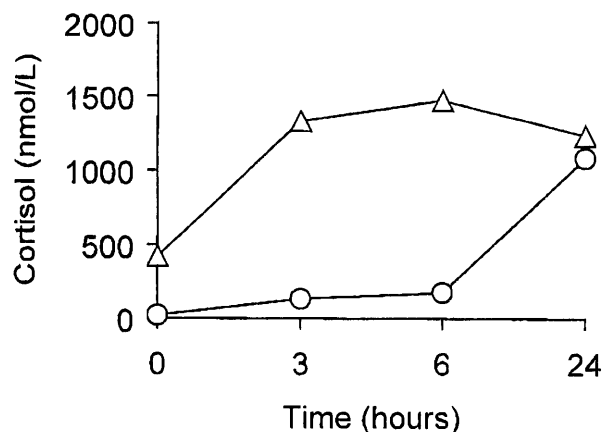


Figure 1 Long tetracosactide test. Mean normal cortisol response (Ref. 4) and patient's response to 2 mg tetracosactide. \triangle Normal; \circ patient

C-reactive protein, potassium and glucose, were normal. Free thyroxine was low at 6 pmol/L, but thyroid stimulating hormone was normal at 2.27 IU/L. The working diagnoses at this point were SIADH and sick euthyroid syndrome.

The patient was admitted and the prochlorperazine was stopped. CT scans of the brain, thorax, pancreas, adrenals and the remainder of the abdomen were normal, as were findings on upper gastrointestinal tract endoscopy. He was fluid-restricted to 1 L per day and over nine days his sodium climbed to 137 mmol/L. The gait and speech disturbance rapidly resolved. When his fluid intake was lifted to 2 L/day, plasma sodium fell to 128 mmol/L and his symptoms began to relapse. A short tetracosactide (Synacthen) test gave the following results: at 0 min, cortisol < 30 nmol/L, corticotropin < 5 nmol/L; at 30 min and 60 min, cortisol 131 and 174 nmol/L, respectively. A long tetracosactide test gave a flat early cortisol response to 2 mg tetracosactide with a delayed peak after 24 h (Figure 1). An MRI scan of

the brain and pituitary showed no abnormalities. Luteinizing hormone, follicle stimulating hormone, testosterone and prolactin levels were normal. A glucagon test suggested growth hormone deficiency. Secondary adrenal insufficiency was diagnosed and the patient's symptoms of fatigue, myalgia and nausea all responded to hydrocortisone replacement therapy. His prostatic symptoms also resolved. Plasma sodium became normal despite a fluid intake in excess of 3 L/day, and the thyroid dysfunction resolved without thyroxine treatment.

COMMENT

SIADH should not be diagnosed until hypoadrenalism has been excluded¹. The long tetracosactide test in this patient showed a delayed peak at 24 h which was diagnostic of secondary adrenal insufficiency. Preservation of mineralocorticoid function in this condition prevents the salt and water depletion seen in Addison's disease. In secondary adrenal insufficiency, hypocortisolism results in increased vasopressin secretion² and an impairment of renal excretion of a water load independent of vasopressin effects³—hence the hyponatraemia. In the case presented here, cortisol deficiency also caused sick euthyroid syndrome.

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